Age-related behavioral phenotype of an astrocytic monoamine oxidase-B transgenic mouse model of Parkinson's disease.

Journal: PLoS One

Publication Year: 2013

Authors: Christopher A Lieu, Shankar J Chinta, Anand Rane, Julie K Andersen

PubMed link: 23326597

Funding Grants: CIRM Research Training Program in Stem Cells and Aging

Public Summary:
We have previously shown that increases in astrocytic monoamine oxidase-B (MAO-B) expression, mimicking that which occurs with aging and in neurodegenerative disease, in a doxycycline (dox)-inducible transgenic mouse model evokes neuropathological similarities to what is observed in the human parkinsonian brain. Additional behavioral and neuropathological studies could provide further validation for its usage as a model for Parkinson's disease (PD). In the present study, we utilized a battery of behavioral tests to evaluate age-related phenotype in this model. In the open field test, we found that dox-induction impaired motor ability with decreases in movement and ambulatory function as well as diminished stereotypical, repetitive movement episodes in both young and old mice. Older mice also showed decreased motor performance in the pole test when compared to younger mice. Furthermore, dox-induced older mice displayed severe hindlimb clasping and the most significant loss of dopamine (DA) in the striatum when compared to young and non-induced animals. Additionally, increased MAO-B activity significantly correlated with decreased expression of striatal DA. The results of our study further confirms that the dox-inducible astrocytic MAO-B transgenic mouse displays similar age-related behavioral and neuropathological features to other models of PD, and could serve as a useful tool to study PD pathophysiology and for the evaluation of therapeutic interventions.

Scientific Abstract:
We have previously shown that increases in astrocytic monoamine oxidase-B (MAO-B) expression, mimicking that which occurs with aging and in neurodegenerative disease, in a doxycycline (dox)-inducible transgenic mouse model evokes neuropathological similarities to what is observed in the human parkinsonian brain. Additional behavioral and neuropathological studies could provide further validation for its usage as a model for Parkinson's disease (PD). In the present study, we utilized a battery of behavioral tests to evaluate age-related phenotype in this model. In the open field test, we found that dox-induction impaired motor ability with decreases in movement and ambulatory function as well as diminished stereotypical, repetitive movement episodes in both young and old mice. Older mice also showed decreased motor performance in the pole test when compared to younger mice. Furthermore, dox-induced older mice displayed severe hindlimb clasping and the most significant loss of dopamine (DA) in the striatum when compared to young and non-induced animals. Additionally, increased MAO-B activity significantly correlated with decreased expression of striatal DA. The results of our study further confirms that the dox-inducible astrocytic MAO-B transgenic mouse displays similar age-related behavioral and neuropathological features to other models of PD, and could serve as a useful tool to study PD pathophysiology and for the evaluation of therapeutic interventions.